

We claim:

1. A hybrid antibody molecule, comprising:

at least one light chain variable region comprising all three complementarity  
5 determining region (CDR's) from a donor immunoglobulin and a light chain variable  
region framework from an acceptor immunoglobulin; and

at least one heavy chain variable region selected from the group consisting of:

(a) a heavy chain variable region which is at least 95% identical to the heavy  
chain variable region of the donor immunoglobulin; and

10 (b) a heavy chain variable region from the donor immunoglobulin.

2. The hybrid antibody molecule of claim 1, wherein the acceptor immunoglobulin  
is a human immunoglobulin.

15 3. The hybrid antibody molecule of claim 1, wherein the heavy chain variable region  
is a fully rodent immunoglobulin sequence.

4. The hybrid antibody molecule of claim 1, wherein the light chain variable region  
is a humanized or a CDR-grafted immunoglobulin chain.

20 5. The hybrid antibody molecule of claim 1, wherein the heavy chain variable region  
is a chimeric chain.

25 6. The hybrid antibody molecule of claim 1, which binds to an antigen with an  
affinity constant between  $10^8 \text{ M}^{-1}$  and  $10^{10} \text{ M}^{-1}$ .

7. The hybrid antibody molecule of claim 1, which comprises two heavy chains and  
two light chains.

8. The hybrid antibody molecule of claim 1, which comprises a constant region selected from the group consisting of kappa, lambda, alpha, gamma, delta, epsilon and mu constant region genes.

5 9. The hybrid antibody molecule of claim 8, wherein the heavy chain or the light chain constant region is from human origin.

10 10. The hybrid antibody molecule of claim 8, wherein the heavy chain constant region is of a human isotype selected from the group consisting of IgG1, IgG2, IgG3, IgG4, IgM, IgA1, IgA2, IgAsec, IgD, and IgE.

11. The hybrid antibody molecule of claim 8, wherein the heavy chain constant region is of human isotype IgG1.

15 12. The hybrid antibody of claim 1, which binds to an immune cell antigen.

13. The hybrid antibody molecule of claim 12, wherein the immune cell antigen is selected from the group consisting of CD1, CD2, CD3, CD4, CD5, CD8, CD18, CD20, CD23, CD40L, CD80, and CD86.

20 14. The hybrid antibody molecule of claim 12, wherein the immune cell antigen is a chemokine receptor selected from the group consisting of a CXC chemokine receptor and a CC chemokine receptor.

25 15. The hybrid antibody molecule of claim 14, wherein the CC chemokine receptor is selected from the group consisting of a CCR1, CCR2A, CCR2B, CCR3, CCR4, CCR5, CCR6, CCR7, CCR8 and CCR9.

16. The hybrid antibody molecule of claim 1, which binds to a tumor antigen.

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17. The hybrid antibody molecule of claim 16, wherein the tumor antigen is selected from the group consisting of EGFR, Her2/neu, HELP, GCC, PSMA, PSA, CD66-c, prostaticin, TMPRSS3, TADG 12 and TADG 15.

5 18. A hybrid antibody molecule, comprising at least one humanized or CDR-grafted light chain variable region and at least one chimeric heavy chain.

19. An anti-CD3 hybrid antibody molecule, comprising:  
at least one light chain variable region comprising all three CDR's from a first  
10 donor species immunoglobulin and a light chain variable region framework from an acceptor immunoglobulin; and

at least one heavy chain variable region selected from the group consisting of:  
(a) a heavy chain variable region at least 95% identical to the heavy chain  
variable region of the donor immunoglobulin; and

15 (b) a heavy chain variable region from the donor immunoglobulin.

20. The anti-CD3 antibody molecule of claim 19, wherein the donor is a rat or a mouse.

20 21. The anti-CD3 antibody molecule of claim 19, wherein the heavy chain variable region has at least one CDR selected from the group of amino acid sequences of SEQ ID NOs:1, 2, and 3.

22. The anti-CD3 antibody molecule of claim 20, wherein the light chain variable  
25 region has at least one CDR selected from the group of amino acid sequences of SEQ ID NOs:4, 5, and 6.

23. The anti-CD3 antibody molecule of claim 19, wherein the heavy chain variable  
framework region has at least one amino acid sequence selected from the group of  
30 consisting of SEQ ID NOs:7, 8, 9, and 10.

24. The anti-CD3 antibody molecule of claim 19, wherein the light chain variable framework region has at least one amino acid sequence selected from the group of consisting of SEQ ID NOs:11, 12, 13, and 14.

5 25. The anti-CD3 antibody molecule of claim 19, wherein the heavy chain variable region has the amino acid sequence shown in SEQ ID NO:17.

26. The anti-CD3 antibody molecule of claim 19, wherein the light chain variable region has the amino acid sequence shown in SEQ ID NO:15.

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27. The anti-CD3 antibody molecule of claim 19, wherein the light chain variable region is linked to a human type lambda constant region.

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28. The anti-CD3 antibody molecule of claim 19, wherein the heavy chain variable region is linked to a heavy chain constant region of an IgG1 isotype.

29. The anti-CD3 antibody molecule of claim 19, wherein the heavy chain constant region is aglycosylated.

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30. The anti-CD3 antibody molecule of claim 29, wherein the asparagine residue at position 297 of the constant region is modified.

31. A pharmaceutical composition comprising the hybrid antibody molecule of either claim 1 or 19, and a pharmaceutically acceptable carrier.

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32. A first and second nucleic acid sequences encoding heavy and light chain variable regions, respectively, of a hybrid antibody molecule,

wherein the heavy chain variable region from a donor immunoglobulin; and

wherein a light chain variable region comprises all three CDR's from a donor

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immunoglobulin and a light chain variable region framework from an acceptor immunoglobulin.

33. A method of providing a modified antibody preparation having improved assembly characteristics, comprising:

providing a first nucleic acid encoding a heavy chain variable region selected from the group consisting of:

(a) a heavy chain variable region at least 95% identical to the heavy chain variable region of a donor immunoglobulin; and

(b) a heavy chain variable region from the donor immunoglobulin;

providing a second nucleic acid encoding a light chain variable region comprising all three CDR's from a donor immunoglobulin and a light chain variable region framework from an acceptor immunoglobulin; and

introducing said first and second nucleic acids into a host cell under conditions that allow expression and assembly of said light and heavy chain variable regions.

34. The method of claim 33, wherein the first and second nucleic acids are linked or unlinked.

35. The method of claim 33, wherein the host cell is a mammalian cell.

36. The method of claim 35, wherein the mammalian cell is selected from the group consisting of a lymphocytic cell line, CHO, COS cells, and a cell from a transgenic animal.

37. A method of modulating the activity of an immune or a cancer cell, comprising contacting the cell with the hybrid antibody molecule of either claim 1 or 19, such that the activity of the cell is modulated.

38. A method of treating or preventing an immune or a cancer disorder, comprising administering to a subject the hybrid antibody molecule of either claim 1 or 19, in an amount effective to treat or prevent the disease.

39. A method for detecting the presence of an antigen recognized by a hybrid antibody molecule in a sample, comprising:

(i) contacting a sample or a control sample with a labeled hybrid antibody molecule of either claim 1 or 19, under conditions that allow interaction of the antibody and the antigen to occur, and

(ii) detecting formation of a complex,

wherein a statistically significant change in the formation of the complex between the labeled hybrid antibody and the antigen with respect to a control sample is indicative the presence of the antigen in the sample.

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